

Fertility-sparing operation for recurrence of uterine cervical perivascular epithelioid cell tumor

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Abstract

Perivascular epithelioid cell tumors (PEComa) are mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelial cells. Although the uterine corpus seems to be one of the most prevalent sites of involvement, PEComa of the uterine cervix are very rare. Only four cervical PEComa cases have been described, and were treated with hysterectomy and radiotherapy.

We report a case of a 24-year-old nulligravida woman who presented with acute abdominal pain and was diagnosed with a rupture of an ovarian chocolate cyst. Subsequent surgery revealed that the tumor arose in the uterus, and the histological diagnosis was uterine PEComa with low potential malignancy. Recurrent PEComa in the uterine cervix were excised twice, and she remains disease free 12 months after the last operation. To the best of our knowledge, this is the first report of recurrent cervical PEComa with fertility-preserving surgery. Estimating the malignant potential and appropriate surgery are essential for young patients with uterine PEComa.

Introduction

Perivascular epithelioid cell tumors (PEComa) are rare mesenchymal neoplasms that include angiomyolipoma, lymphangiomyomatosis, clear cell tumor of the lung (CCTL), and a set of similar visceral and soft tissue lesions that are all characterized by "perivascular epithelioid cells" concentrated around the tumor blood vessels. This particular subgroup is very rare, and has been reported in several organs such as the uterus, lung, kidney, liver, small and large bowel, and prostate. In previous reports of uterine PEComa, the mean age of patients was 45 years old, the predominant location was the corpus, and most patients were treated with hysterectomy. Only four cases of cervical PEComa have been

reported.² Here, we report recurrent cervical PEComa in a young woman treated with fertility-preserving operations.

Case Report

A 24-year-old Japanese nulligravida woman, with no history of tuberous sclerosis, was diagnosed with an ovarian chocolate cyst and treated for three months with gonadotropin-releasing hormone analogue (GnRHa). Five months later, an emergency laparotomy was performed under a preoperative diagnosis of ruptured ovarian cyst because of sudden severe abdominal pain and massive ascites. Bloody ascites measured 700 mL; both ovaries were normal but the uterus had a 4 cm myoma on the left dorsal side. Membranous tissue similar to endometriosis was removed from the surface of the uterus and was diagnosed pathologically as PEComa.

Four months after the operation, the patient visited our hospital with suspected recurrent PEComa. Magnetic resonance imaging (MRI) demonstrated a 26×50×59 mm cyst behind the uterus (Figure 1A), but the computed tomography (CT) scan showed no metastasis. A laparotomy was performed under the diagnosis of recurrent PEComa. The uterus had a flat tumor 10 cm in diameter on the left side of the cervix (Figure 1B), and marked bloody ascites in the closed Douglas pouch. The tumor was resected and histological examination revealed a spindle cell tumor with some epithelioid cells. The tumor cells had round to oval nuclei with small but prominent nucleoli, and abundant eosinophilic cytoplasm (Figure 1C). Infiltrating patterns of growth were observed, showing a tongue-like pattern of the tumor extending into the surrounding stroma and a net-like pattern with hyalinized stroma. Immunohistochemical staining showed tumor cells strongly positive for HMB-45 (Figure 1D), and partially or weakly positive for CD34 and factor VIII. AE1/3, S-100, c-kit, smooth muscle actin (SMA), desmin, CD31, and CD1a were negative in the specimens tested. The proliferation marker MIB-1 was immunoreactive in 2-3% of tumor cells. Therefore, this tumor was diagnosed as recurrent PEComa of the uterine cervix with low-grade malignancy.

Seven months after the second operation, the patient suffered prolonged menstrual bleeding and slight abdominal pain. MRI revealed a 10×14 mm defect in the left-side wall of the uterine cervix and hemorrhage in the Douglas pouch. A third laparotomy was performed after GnRHa treatment for six months, and a myometrial defect, 15 mm in diameter, was found on the left side of the cervix. The uterine wall was sutured after debridement and the resected tissue was diagnosed immunohistochemically as recurrent PEComa.

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At the most recent follow-up 12 months later, there was no evidence of recurrence.

Discussion

PEComa are characterized by an epithelioid morphology, clear to eosinophilic granular cytoplasm, coexpression of smooth muscle (actin and/or desmin) and melanocytic markers (HMB-45 and/or melanA), and at least in some cases, arrangement around blood vessels.^{2,3} However, in our case tumor cells expressed HMB-45 strongly, but no smooth muscle markers. Uterine epithelioid mesenchymal tumors composed of cells that expressed HMB-45 were classified as PEComa, regardless of the absence or presence of muscle markers.^{2,4} The immunophenotypic profile of the uterine PEComa showed that positivity for SMA and desmin was not 100%, but greater than 70% and almost half, respectively.^{2,4,5} Vang *et al.*⁴ divided PEComa of the uterus into two groups (A and B) morphologically, and the muscle marker expression was scanty in group A but extensive in group B. These reports suggested that PEComa are a subset of HMB-45 positive epithelioid mesenchymal tumors of the uterus with an uncertain relationship to pure smooth muscle tumors.

It is important to distinguish PEComa from other mesenchymal tumors. In most cases,

clear cell sarcomas can be distinguished from PEComa by virtue of their strong expression of S-100 protein and nonimmunoreactivity with SMA.¹ It was reported recently that CD1a expression may be a useful immunohistochemical adjunct in the diagnosis of uterine PEComa, distinguishing them from uterine epithelioid smooth muscle tumors,^{6,7} but our case was negative for SMA as well as for CD1a. For endothelial markers, the tumor cells in our case were weakly or partially positive for CD34 and factor VIII, but negative for CD31. There are only a few reports that showed the results of immunoreactivity with CD34 in endothelial markers, and CD34 positivity was seen in 5% of the uterine PEComa cases.⁵ Gastrointestinal stromal tumors (GISTs) may also enter the differential diagnosis of PEComa, as both tumors show a mixture of epithelioid and spindle morphology. CD34, which is positive in GISTs, may be useful in this differential diagnosis.¹ However, PEComa differ from GISTs in that they typically show clear to light eosinophilic cytoplasm. These findings suggest that the diagnosis of PEComa should be performed comprehensively with morphological and immunophenotypical features.

Forty-six uterine PEComa cases had been reported in the English literature by November 30, 2009;² however, 42 cases arose in the corpus and four in the cervix,^{1,8,9} and our case is the fifth report of cervical PEComa (Table 1). In cervical PEComa, patients were younger than in corpus PEComa cases (cervical, 33.2 ± 10.7 ; corpus, 45.3 ± 14.7), with recurrence occurring only in our case and no mortality reported, whereas nine patients showed recurrence and four died in the 42 corpus PEComa cases. However, cervical PEComa are so rare that it cannot be determined whether the prognosis of cervical PEComa is better than that of corpus PEComa.

Our case recurred twice in the uterine cervix, but the tumor was resected only to preserve fertility. Three previously reported cervical PEComa were treated with hysterectomy, and one with radiotherapy, possibly because excision is more difficult for tumors of the cervix than of the corpus owing to their length and location. In 46 uterine PEComa, four corpus PEComa were treated only with excision, and the outcomes of the three available cases showed that one had recurrent lymph node metastasis but all were cured.

The malignant potential of PEComa varies and this can be determined by mitotic activity, cellularity, nuclear grade, etc.¹ Our case was diagnosed as PEComa with low-grade malignancy because the proliferation marker MIB-1 was immunoreactive in 2-3% of tumor cells. The mitotic rate and labeling index for MIB-1 (Ki-67) are useful to determine the malignant

Table 1. Reported cases of uterine cervical perivascular epithelioid cell tumors.

Case	Age	History of pregnancy	Management	Malignancy	Outcome	Reference
1	28	NS	Hysterectomy, lymphadenectomy	MI 0/50HPF	NED 36 m	1
2	48	NS	Adjuvant radiotherapy	MI 0/50HPF	NED 21 m	1
3	25	Multiparous	Radical hysterectomy, lymphadenectomy	NS	NS	8
4	41	Gravid-1 Para-1	Hysterectomy, BSO	MI <1/50HPF	NED 35 m	9
5	24	Null	Excision	MIB-1 2-3%	Recurrence 4 m and 11 m, NED 12 m	Present

NS, not stated; MI, mitotic index; NED, no evidence of disease; BSO, bilateral salpingo-oophorectomy.

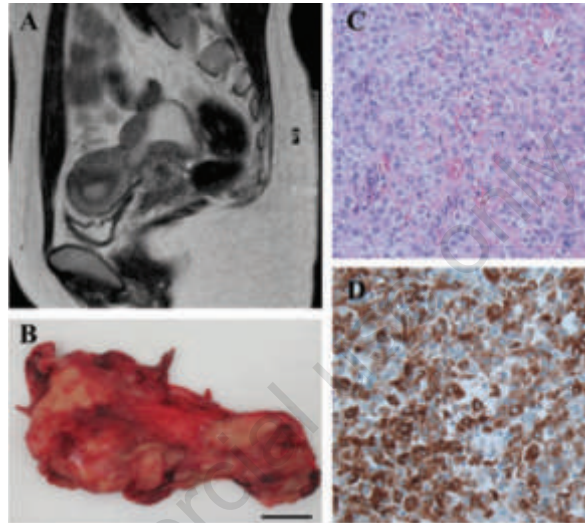


Figure 1. (A) T2-weighted MRI of the pelvis demonstrated a hemorrhage cyst from the uterine cervix. (B) Gross appearance of the tumor was flat, thick, and smooth-surfaced. Scale bar = 2 cm. (C) Histological appearance of the tumor showing a spindle cell tumor with round, swollen nuclei and abundant eosinophilic cytoplasm (hematoxylin and eosin stain; magnification: 100X). (D) Strong reaction of the tumor cells with the melanocytic marker HMB-45 (magnification: 100X).

level, and fertility-sparing operations can be considered for low malignant uterine PEComa.

References

- Folpe AL, Mentzel T, Lehr HA, et al. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. *Am J Surg Pathol* 2005; 29:1558-5.
- Fadare O. Uterine PEComa: appraisal of a controversial and increasingly reported mesenchymal neoplasm. *Int Semin Surg Oncol* 2008;5:7.
- Bonetti F, Pea M, Martignoni G, et al. PEC and sugar. *Am J Surg Pathol* 1992;16:307-8.
- Vang R, Kempson RL. Perivascular epithelioid cell tumor ("PEComa") of the uterus: a subset of HMB-45-positive epithelioid mesenchymal neoplasms with an uncertain relationship to pure smooth muscle tumors. *Am J Surg Pathol* 2002;26:1-13.
- Fadare O. Perivascular epithelioid cell tumor (PEComa) of the uterus: an outcome-based clinicopathologic analysis of 41 reported cases. *Adv Anat Pathol* 2008; 15:63-75.
- Adachi Y, Horie Y, Kitamura Y, et al. CD1a expression in PEComas. *Pathol Int* 2008; 58:169-73.
- Fadare O, Liang SX. Epithelioid smooth muscle tumors of the uterus do not express CD1a: a potential immunohistochemical adjunct in their distinction from uterine perivascular epithelioid cell tumors. *Ann Diagn Pathol* 2008;12:401-5.
- Azad NS, Aziz AB, Pervez S, et al. Uterine perivascular epithelioid cell tumour presenting as a cervical mass. *J Pak Med Assoc* 2006;56:83-4.
- Fadare O, Parkash V, Yilmaz Y, et al. Perivascular epithelioid cell tumor (PEComa) of the uterine cervix associated with intra-abdominal "PEComatosis": A clinicopathological study with comparative genomic hybridization analysis. *World J Surg Oncol* 2004;2:35.